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Brucellosis in childhood in the Western Cape

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Human brucellosis, a multisystem disease which may mimic other conditions, has a low incidence in childhood and the diagnosis may easily be missed. Over a 7-month period 9 children with brucellosis presented to the Department of Paediatrics and Child Health, Tygerberg Hospital. Six of the children had consumed unpasteurised milk. The main presenting symptoms were fever, fatigue, headache, myalgia and haematuria. Clinical signs included lymphadenopathy (3), nasopharyngitis (2), features of lower respiratory tract infection (2), splenomegaly (2) and pyrexia (1). The diagnosis was made on the basis of a positive serological titre (> 1:160) for *Brucella abortus*. The prozone phenomenon was encountered in 6 cases; however, the Coombs test confirmed the diagnosis in these cases. Children under 7 years were treated with co-trimoxazole and rifampicin and those over 7 years with tetracycline and rifampicin, for at least 6 weeks. No relapses were detected on follow-up.

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Brucellosis, a zoonosis with a worldwide distribution, is caused by Gram-negative organisms belonging to the genus *Brucella* of which there are six species. The four species that cause disease in man are *Brucella abortus* (cows and camels), *B. mellitensis* (goats), *B. suis* (pigs) and *B. canis* (dogs). Man is infected by consumption of unpasteurised milk or dairy products or through handling of contaminated meat.[1] The incidence of brucellosis in South Africa is low compared with other parts of the world such as Central and South America, southern Europe, the rest of Africa, the Middle East and central Asia, where the disease is a serious public health problem.[2] Brucellosis appears to be rare in childhood.[2,3] For 10 years prior to this report only 1 child with the disease was treated by us. We report on the clinical presentation, diagnosis and treatment of 9 children with brucellosis seen over a 7-month period at Tygerberg Hospital.

Material and methods

The sample included children 14 years of age or younger seen at Tygerberg Hospital between 1 August 1992 and 27 February 1993. A diagnosis of brucellosis was suggested by the clinical picture and confirmed by positive serological findings based on the tube agglutination test. This entailed serial dilutions of the patient's serum to which *Brucella* suspension (Wellcome) was added. After overnight incubation at 37°C the tubes were assessed for agglutination the next day. A titre of 160 or greater or a fourfold rise in titre was considered positive. A Coombs test was done in the event of the prozone phenomenon (a negative reaction obtained with serum that has a high antibody titre). In all patients serological investigations were undertaken on initial presentation and in 8 cases at follow-up 1 - 4 months later. Blood cultures and liver function tests were done on 7 of the 9 patients. C-reactive protein levels or erythrocyte sedimentation rates were ascertained in 6. Full blood and differential counts were determined in all the patients.

Results

There were 9 children with the diagnosis of brucellosis. Two lived in urban and 7 in rural areas. Five of the children were from two families, in which the parents were also infected. A history of having drunk unpasteurised milk was elicited in 6 cases. Health inspectors were unsuccessful in uncovering the source of the infection. The clinical and laboratory findings of the children are summarised in Table I. There were 3 boys and 6 girls and their ages ranged from 1½ to 14 years. The main presenting symptoms were fever (6), arthralgia and myalgia (5), headache (5), fatigue (5) and haematuria (1). In the child presenting with haematuria, the diagnosis was made after an extensive search for the cause. The physical findings in the patients were sparse and variable. They included lymphadenopathy (3), nasopharyngitis (3), lower respiratory tract infection (2), splenomegaly (2) and pyrexia (1).

Laboratory investigations did not provide clues to the diagnosis. Two children had leucopenia and 1 had leucocytosis. The haemoglobin and platelet counts were normal. C-reactive protein levels were raised in 2 and the

erythrocyte sedimentation rate in another. Liver function tests were normal in all 7 of the patients tested. Titres for *Brucella abortus* ranged from 160 to 1 280. In 2 of the children (patients 6 and 7, Table I) positive titres for both *B. abortus* and *B. mellitensis* were found which probably resulted from cross-reactions. In 6 cases the prozone phenomenon was encountered. However, the Coombs test for *Brucella* was positive. Blood cultures done in 7 cases were all negative for brucellosis. Children under 7 years of age were treated with co-trimoxazole and rifampicin and those over 7 years with tetracycline and rifampicin for at least 6 weeks. Three of the children were initially hospitalised. Six were diagnosed and treated on an outpatient basis. No complications were encountered. At follow-up 4 months after therapy, all were asymptomatic.

Discussion

Childhood brucellosis has long been considered an uncommon disease as children make up less than 10% of all cases.[4] The reported low childhood incidence has been attributed to the following: (*i*) other diseases have similar manifestations; (*ii*) in children the disease is mild compared with adults; (*iii*) brucellosis is infrequently considered in childhood; and (*iv*) adults working with livestock or in meat-processing industries have a high risk of exposure to the disease.[2,3,5]

In South Africa, the incidence of brucellosis appears to be low (Fig. 1).[6] However, there is underreporting so that this is not an index of the disease's true incidence. Outbreaks of brucellosis in the Transkei, Eastern Cape and Orange Free State, accounted for the higher incidence between 1981 and 1986 (Directorate: Epidemiology, DNHPD — personal communication). The increased number of cases reported in 1992 relative to the preceding 5 years suggests another outbreak of disease following a breakdown in herd surveillance.

The clinical manifestations of brucellosis are protean and the severity of the disease depends on the *Brucella* species. *B. mellitensis* is more pathogenic than the other species and produces more intense symptoms.[5,7-9] The children in this series appeared to have been infected with *B. abortus*. Their symptoms were nonspecific but demonstrate the

Table I. Clinical and laboratory data on brucellosis cases

		Clinical findings			Laboratory findings (A = admission; mo. = follow-up)		
Patient	Age (yrs)	Symptoms	Signs	WCC/diff (x 10^9/l)	CRP (µg/ml), ESR (mm/h)	Agglutinins	Coombs
1	14	Headache Arthralgia Myalgia Fatigue	Cervical adenopathy Splenomegaly Pharyngitis	3,9/55 N 32 L 6 M	Neg	*B.ab* = 1:160 (A) *B.ab* = 1:40 (4 mo.)	
2	4	Fever Arthralgia Myalgia Fatigue	LRI	6,2/32 N 56 L 5 M	Not done	*B.ab* neg	*B.ab* 1:160 (A) 1:80 (2 mo.) 1:40 (4 mo.)
3	12	Fever Arthralgia Myalgia Headache Fatigue	Nasopharyngitis	3,4/45 N 37 L	Not done	*B.ab* neg	*B.ab* 1:160 (A) 1:80 (2 mo.) 1:80 (4 mo.)
4	12½	Fever Arthralgia Myalgia Headache Fatigue	Nasopharyngitis	5,5/39 N 45 L 9,6 M 6 E	Neg	*B.ab* neg	*B.ab* 1:160 (A) neg (2 mo.) neg (3 mo.)
5	11	Fever Headache Fatigue	Nasopharyngitis	7,3/36 N 47 L 7 M	Neg	*B.ab* neg	*B.ab* > 1:160 (A) 1:80 (2 mo.) 1:40 (4 mo.)
6	9½	Fever Arthralgia Myalgia Headache	None	8,3/40 N 40 L 12 M	ESR = 45	*B.ab* = 1:1052 (A) *B.mell* = 1:1052 (A) *B.ab* = 1:40 (1 mo.) *B.mell* = 1:10 (1 mo.)	Neg
7	4½	Abd. pain Haematuria	Urine = 4 + blood (dipstick)	13/60 N 26 L 8 M 3 E	Not done	*B.ab* = 1:20 *B.mell* = 1:20 *B.ab* neg (4 mo.)	*B.ab* > 1:160 (A) *B.mell* > 1:160 (A)
8	4½	Fever Previous UTI	Pyrexia Cervical adenopathy	26/60 N 27 L 9 M	CRP = 79	*B.ab* = 1:160(A)	
9	1½	Cough Swelling in neck	Cervical adenopathy Splenomegaly LRI	13 ND	CRP = 67	*B.ab* neg	*B.ab* > 1:1280 (A) *B.ab* = 1:40 (2 mo.)

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; WCC = white cell count; diff = differential count; LRI = lower respiratory infection; *B.ab* = *Brucella abortus*; *B.mell* = *Brucella mellitenis*; N = neutrophils; L = lymphocytes; M = monocytes; E = eosinophils; UTI = urinary tract infection; ND = not done.

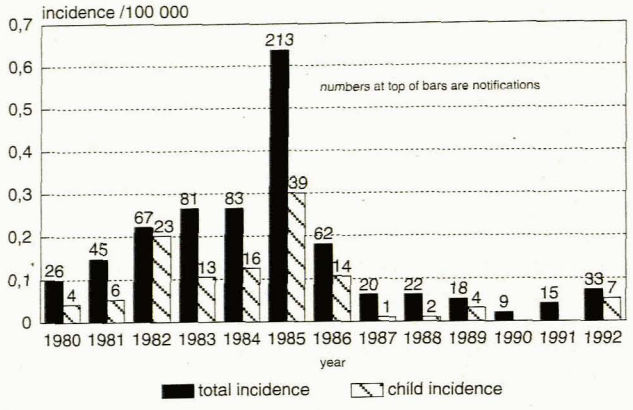

Fig. 1. Brucellosis incidence and notifications, 1980-1992.

importance of considering the diagnosis in children presenting with fever, arthralgia, weight loss and malaise.[5,10,11] There may occasionally be urinary symptoms such as haematuria, as was the case in 1 of our patients. The clinical findings of brucellosis are sparse, but may include cervical and axillary lymphadenopathy, hepatosplenomegaly and polyarthritis of the large joints. None of our children had polyarthritis but the other features were present. In 2 cases the illness was complicated by pneumonia but other complications such as meningo-encephalitis, endocarditis, pleural effusion, visceral abscesses, osteomyelitis and suppurative arthritis were not encountered.[9]

The haematological findings in children with brucellosis are diverse. Anaemia is an inconstant feature of the disease[5] and was not present in any of our patients. Leucopenia with a relative lymphocytosis, although well described in adults, is rare in children[4,12] and only 2 of our children had leucopenia and none had pancytopenia which has been described in brucellosis.[5,11,13] Raised hepatic transaminase levels are described in association with hepatic enlargement[3,5] but were not found in any of our patients. Raised C-reactive protein levels, although a useful adjunct in the diagnosis, particularly in non-arthritic brucellosis,[8] were present in only 2 of 5 of the children tested.

The diagnosis of brucellosis is based on epidemiological evidence of a source of infection, compatible clinical findings and at least one of the following laboratory criteria: isolation of the organism from blood or other tissues, a *Brucella* agglutination titre of ≥ 160 or a fourfold rise in titre following the onset of symptoms.[2,5,9,12] Laboratory culture of *Brucella* is difficult because the organism is slow-growing and requires enriched media and high CO_2 tension.[9,12] Serological investigation is therefore valuable in diagnosis but the tube agglutination test may be negative due to the prozone phenomenon in which blocking antibodies of the IgG and IgA classes are present. This can be obviated if dilutions are carrried out to a titre of 1:1 280 or the Coombs test is done.[4,9,12] In our study the diagnosis would have been missed in 6 cases if the Coombs test had not been done.

Current recommendations for treatment include combination therapy with two drugs continued for a minimum of 6 weeks. Single-drug therapy has an unacceptable relapse rate. In children 8 years of age or more a tetracycline, e.g. doxycycline 100 mg twice daily, and rifampicin 15 mg/kg (max. 900 mg) daily, and in those 8 years or younger trimethoprim-sulphamethoxazole 30 - 60 mg (total drug with 1 part trimethoprim to 5 parts sulphamethoxazole) in divided doses twice daily and rifampicin 15 mg/kg/day are recommended.

In South Africa, brucellosis is controlled in terms of the Animal Diseases Act (Act No. 35 of 1984). More than 20% of herds in the country are infected, with regional variations in the infectivity rate. Preventive measures employed include routine vaccination of heifers aged between 4 and 8 months, monthly testing of milk by a milk ring test and purchase of new stock certified free from disease. While numerous programmes exist to control the disease, participation is voluntary. Poor control and the sale of unpasteurised milk indicate that major epidemics in South Africa are a real threat in future.[14,15]

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